Received: 19 April 2019 | Accepted: 23 August 2019

DOI: 10.1002/jcp.29142

Journal of Cellular Physiology WILEY

ORIGINAL RESEARCH ARTICLE

CD93 hematopoietic stem cells improve diabetic wound healing by VEGF activation and downregulation of DAPK-1

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Abstract

Diabetes is associated with numerous complications, such as diabetic skin wounds or ulcerations. The aim of this study was to evaluate experimentally the effectiveness of applying polycaprolactone (PCL)-gelatin scaffold, with or without rat CD93 hematopoietic stem cells (HSCs), in diabetic wound healing in a rat model. CD93 HSCs were aseptically isolated from rat bone marrow using fluorescent activated cell sorting (FACS) method and FACS-SORTER. A total of 25 Wistar rats were divided into five groups including Group I (sham, nondiabetic, and wound covered only with sterile dressing), II (control, diabetic rat), III (CD93 HSCs alone), IV (PCL-gelatin scaffold), and V (CD93 HSCs+PCL-gelatin scaffold). Animals were killed on Days 7, 14, or 28 posttreatment and histological sections were blindly evaluated by two expert pathologists. Death-associated protein kinase 1 (DAPK-1) gene and vesicular endothelial growth factors (VEGF) protein expression were evaluated using reverse transcription-polymerase chain reaction and western blot, respectively. The thickest and the thinnest epidermises microscopically were belonged to CD93+HSCs+scaffold and the control group, respectively. The growth rate of the epidermis and adnexal epithelia was the highest in both the cell and cell+scaffold groups. Evaluation of the protein expression level of VEGF indicated that the expression levels of this growth factor were the most on Day 7 posttreatment in sham, HSCs alone, and HSCs cell +scaffold groups. While the lowest expression levels of this growth factor was detected in the control and scaffold groups. The gene expression level of DAPK-1 on Day 7 posttreatment was higher than that of the Day 14 posttreatment in all groups. The highest and lowest gene expression levels of DAPK-1 belonged to control and sham groups, respectively. According to our findings, CD93 HSCs offer new prospects for the treatment of diabetic ulcers and concomitant application of these cells with PCL-gelatin nanofiber scaffold significantly improves diabetic wound treatment.

KEYWORDS

CD93, diabetic wound healing, hematopoietic stem cells, PCL-gelatin scaffold

1 | INTRODUCTION

Diabetes is the most common endocrine disorder and the most important metabolic disease in human. It is predicted that the number of people with diabetes will reach 300 million cases worldwide by 2030 (Wild, Roglic, Green, Sicree, & King, 2004). Diabetes is associated with numerous complications, such as peripheral neuropathy, stroke, cardiovascular disease, chronic renal

